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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/672,626	09/26/2003	Amy F.T. Arnsten	MPI-0003	8080

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EXAMINER	
CLAYTOR, DEIRDRE RENEE	
ART UNIT	PAPER NUMBER
1617	

NOTIFICATION DATE	DELIVERY MODE
02/25/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/672,626	ARNSTEN ET AL.	
	Examiner	Art Unit	
	Renee Claytor	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2008*.

2a)☒ This action is FINAL. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,10,12,14,18-20 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4, 10, 12, 14, 18-20, 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/14/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Currently, claims 1, 4, 10, 12, 14, 18-20 and 22 are pending.

Response to Arguments

Applicants response filed on 11/14/2008 have been fully considered. In particular, Applicants have argued that the '450 patent teaches away from oral or systemic administration of PKC inhibitors and the section relied on by the Examiner is specifically directed to in situ applications. Applicant's argue that the '450 patent inventor contemplates the use of pills or capsules for axon regeneration outside the CNS and not for indications that require transfer of PKC inhibitors across the blood brain barrier. Applicants further assert that the mention of pills and capsules cannot form the basis for an obviousness rejection because one of ordinary skill would not have known how to transfer chelerythrine across the blood brain barrier. Because Applicants feel that it is not obvious to administer a PKC inhibitor by oral or systemic administration, they assert that Birnbaum et al. cannot be combined in an obviousness rejection.

In response to the above arguments, the Examiner would like to point to the '450 patent in which it is taught in Col. 3, lines 56-59 that administration of inhibitors of PKC present in the target CNS tissue in *in vivo* systems typically requires surgical or pharmacological methods. Further it is discussed that compositions comprising the inhibitor may be administered in combination with a pharmaceutically acceptable excipient such as sterile saline or other medium, gelatin, an oil, etc. to form

pharmaceutically acceptable compositions (Col. 4, lines 65-67 – Col. 5, line 1). The reference goes on to teach that the compositions or compounds can be formulated with carriers and can be formulated into capsules or pills etc. Therefore the '450 patent does contemplate pharmaceutical formulations for CNS disorders and one would find it obvious that the formulations would be expected to cross the blood brain barrier. Further, the Birnbaum reference is relied upon for the teaching that chelerythrine treats working memory impairment and bipolar disorder. Therefore, it would be obvious to administer the composition as taught by the '450 patent orally to a patient to effectively treat bipolar disorder.

Applicants have amended the claims to overcome the 35 USC 112, first paragraph rejection for written description and the rejection is hereby withdrawn.

Applicants have argued over the 35 USC 112, first paragraph rejection for scope of enablement that claim 20 is enabled because the claim is drawn to a method of preventing manic episodes and not to bipolar disorder in general and have presented a paper to back up their assertion. In response, it is noted that the specification of the current application and the article do not teach total prevention of manic episodes. The term "prevention" is an absolute term in which there would be no occurrence of manic episodes at all. The article presented by the applicant teaches that lithium substantially reduces the risk of relapse to manic episodes by about 40%. Accordingly, the rejection is maintained.

Because Applicant's have amended the claims to include oral and systemic administration, the 35 USC 102 rejection is withdrawn. However, because the claims have been amended the following new grounds of rejection are being made.

Claim Rejections -35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 20 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating learning and memory tasks and mania by administration of chelerythrine, does not reasonably provide enablement for preventing a subject from developing a CNS disorder by administering chelerythrine. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the

art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the invention: The rejected claim 20 is drawn to a method comprising preventing a subject from developing a CNS disorder by administering a pharmaceutical composition.

(2) The state of the prior art: The state of the art regarding treating bipolar disorder is high. However, the state of the art regarding prevention of bipolar disorder is underdeveloped.

(3) The relative skill of those in the art: The relative skill of those in the art is high.

(4) The breadth of the claims: Claim 20 embraces a method comprising preventing a subject from developing bipolar disorder by administering to a subject a pharmaceutical composition.

(5) The amount of guidance or direction presented: In the instant case, working examples are presented for treating manic episodes and learning and memory tasks with chelerythrine in the specification on pages 19-23 in which chelerythrine was shown to increase performance on learning and memory tasks as well as improve the stress response (involving manic episodes). However, there is a lack of working examples presented in the specification as filed showing how to prevent bipolar disorder. Note that lack of a working example is a critical factor to be considered,

especially in a case involving an unpredictable and undeveloped art. See MPEP § 2164.

(6) The presence or absence of working examples: Applicant does not provide any working examples for the prevention of bipolar disorder.

(7) The quantitation of experimentation necessary: Claim 20 reads on a method comprising preventing bipolar disorder by administration of a pharmaceutical composition. As discussed above, the specification provides examples for treating learning and memory disorders and bipolar disorders but the specification fails to provide support for the prevention of bipolar disorder. Applicant fails to provide information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4, 10, 12, 14, 18, 19, 20 rejected under 35 U.S.C. 103(a) as being unpatentable over Birnbaum et al. (Society for Neuroscience Abstract, 2000) in view of He et al. (US Patent 6,815,450).

Birnbaum et al. teach that local intra-PFC infusion of chelerythrine reversed stress-induced working memory impairment caused by phenylephrine in rats. The authors conclude that blockade of PKC may help to restore cognitive function during stress (see whole document).

Birnbaum et al. does not contemplate other modes of administration of chelerythrine.

He et al. teach chelerythrine as a PKC inhibitor and teach in situ applications. He et al. teach that for the in situ applications, compositions comprising the PKC inhibitor may be administered by any effective route compatible with therapeutic activity of the compositions and patient tolerance (Col. 4, lines 3-6). It is further contemplated by the teachings of He et al. that the inhibitor is administered in a pharmaceutically acceptable excipients such as saline or other medium in an effort to form pharmaceutically acceptable compositions and dosage units that may be included in capsules, pills, etc. which contemplates other routes of administration other than local injection (i.e., systemic infusion and oral).

Accordingly, it would be obvious to a person of ordinary skill in the art to treat bipolar disorder or working memory deficit with chelerythrine because of the teachings of Birnbaum et al. that chelerythrine reverses stress-induced working memory impairment. One would be motivated to modify the teachings of Birnbaum et al. to

include other modes of administration, including oral administration, in an effort to effectively administer chelerythrine to a patient in need of restoration of normal cognitive function.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 4, 10, 12, 14, 18-20 and 22 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3-4, 14-15 of copending Application No. 12/086,658. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant invention are drawn to a method of treating bipolar disorder with a composition comprising chelerythrine while the claims of application 12/086,658 are drawn to a method of treating a cognitive or mood disorder comprising administration of an

effective amount of chelerythrine. The claims are not identical in the claims of 12/086,658 are also drawn to administration of guanfacine in combination with chelerythrine.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Renee Claytor whose telephone number is (571)272-8394. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Renee Claytor

/SREENI PADMANABHAN/
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